INFLAMMATORY PSEUDOTUMORS OF THE LUNG: IMPORTANCE OF RECOGNITION AND DIFFERENTIATION FROM NEOPLASTIC AND GRANULOMATOUS PROCESSES

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Two cases of inflammatory pseudotumors of the lung are reported and the literature is reviewed. The lesions are commonly discovered incidently in asymptomatic young persons and are characterized by a solitary, homogeneous, well-circumscribed mass composed of the major kinds of inflammatory elements in various proportions. The lesion should be differentiated from true neoplasms and common granulomas. Resection of the lesion results in permanent cure.

Inflammatory pseudotumors of the lung are rare lesions, commonly characterized by a persistent or slowly growing, solitary lung mass that often masquerades as a neoplasm but proves to be a nonspecific inflammatory process (confirmed by histology), composed predominantly of plasma cells and/or histiocytes.[1-12] Confusion about such an entity has been generated in the past because of the lack of an identifiable causative agent and the multitude of names applied to the lesion based upon its highly variable histologic features.[1-13] It is important to recognize inflammatory pseudotumors of the lung as benign lesions and differentiate them from true neoplasms and common granulomatous processes because, hitherto, no death has been attributed directly to such inflammatory pseudotumors.

Two cases of inflammatory pseudotumors of the lung with different clinical courses and histologic features are presented. In one case the lesion was removed 17 years ago and the patient is still living and well, while in another case, the lesion was not removed but the patient has been closely observed during the past seven years.

CASE REPORTS

Case 1

A 34-year-old man was admitted to the hospital for paranoid behavior of approximately two months' duration. A large left-sided hilar mass with the appearance of a neoplasm was seen on chest x-ray film taken on admission (Figure 1A). The patient's schizophrenic reaction was treated with drugs while a workup of the lung lesion was performed. The left-sided hilar mass measured 6 cm in diameter, and was rather homogeneous, well demarcated, and round on posteroanterior film (Figure 1A) but was obviously lobulated on tomogram (Figure 1B). Skin tests and sputum cultures for tuberculosis and fungal infections were negative. Sputum cytologies, bronchoscopy, and mediastinoscopy were negative for malignancy. An exploratory left-sided thoracotomy was then performed revealing a large

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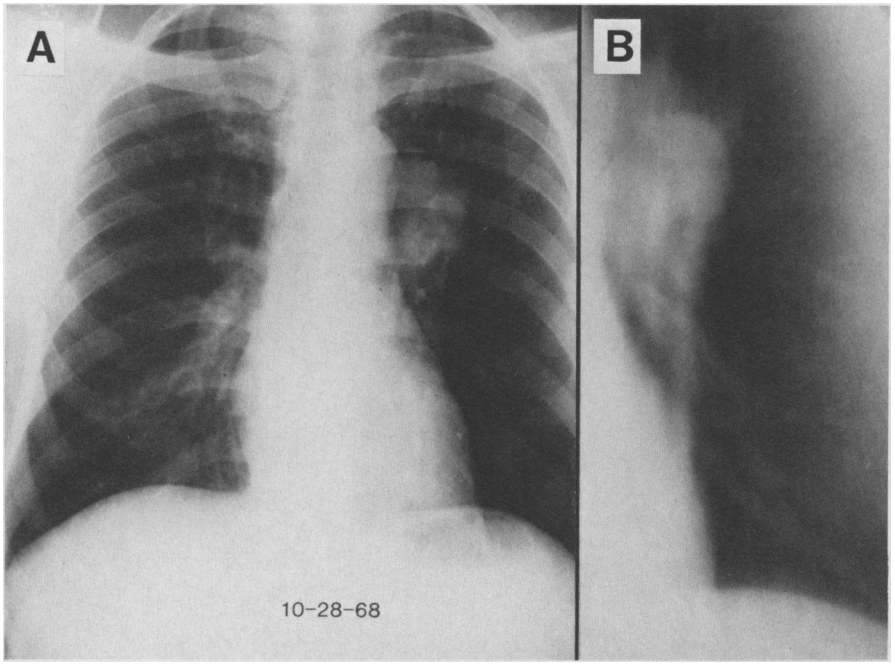

Figure 1. A round, well-demarcated mass in the left hilum (A, posteroanterior film) is revealed on the chest radiograph that is seen as lobulated on tomogram (B)

mass in the anterior segment of the left upper lobe, which protruded into the mediastinum at the level of the lung hilum on the left side. A left-sided pneumonectomy was carried out because a frozen section was reported as suspected malignant disease.

On gross examination the mass in the lung on the left side was slightly lobulated, well defined but not encapsulated, measuring 6 cm in its greatest dimension, and located subpleurally without invasion of the pleura. The cut surfaces were white-grey with scattered yellow and brown spots and small foci of cystic degeneration. The consistency was firm to rubbery. Microscopically, a combination of varieties of the following histologic features was present (Figure 2): lymphocytic infiltrates with occasional germinal centers (Figure 2A), focal neutrophilic and eosinophilic infiltrates, massive aggregates of mature plasma cells with easily identifiable Russell bodies (Figure 2B), granulation tissue composed of capillaries and fibrous tissue (Figure 2C), sheets of epitheloid histiocytes with occasional multinucleated giant cells (Figure 2D), bundles of spindle-shaped histiocytes and collagen arranged in storiform patterns (Figure 2E), loose and dense fibrous tissue, old hemorrhages with hemosiderin deposit and cholesterol granuloma formation and rare, small focal calcifications and small cysts walled-off by chronic inflammatory cells (Figure 2F). The above process seemed to arise from the lung parenchyma and to expand peripherally to the adjacent lung tissue. Special stains and cultures of the lung failed to yield any microorganisms.

The patient recovered from the surgery uneventfully. Subsequently, his schizophrenic reaction was brought under control. Seventeen years later, the patient is living and well, free from recurrent lung lesion.

Case 2

A 32-year-old male construction worker, who has been a binge drinker and two pack-a-day smoker for 15 years, first developed dull, continuous pain in the lower chest on the left side associated with shortness of breath and mild fever in May 1978. Inhomogeneous opacities in the lingula segment of the left upper lobe with elevation of the left-sided hemidiaphragm, consistent with pneumonia, were revealed on a chest radiograph (Figure 3B). A previous chest film, taken in March

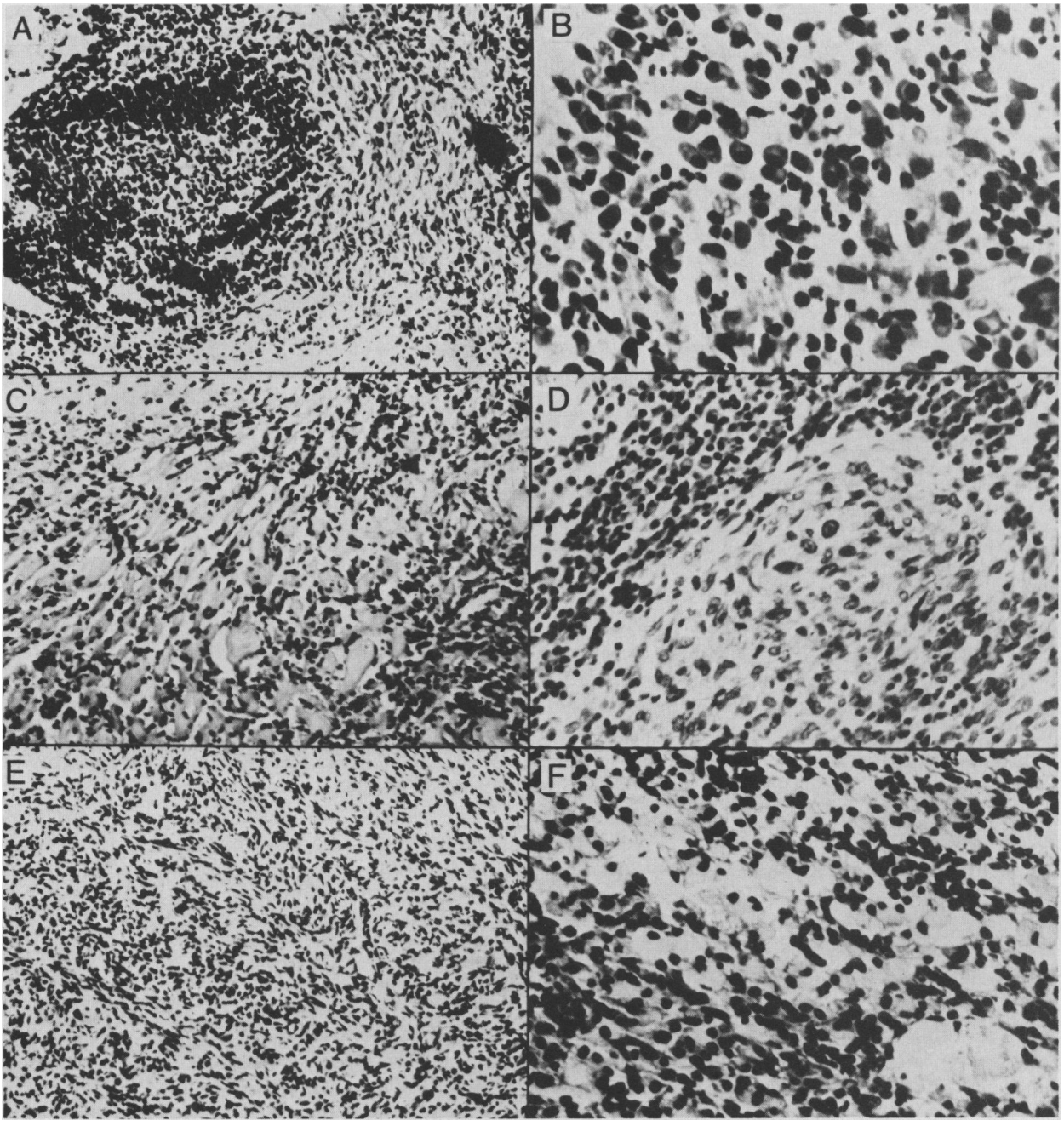

Figure 2. A wide spectrum of histologic features characterizing the inflammatory pseudotumors in case 1: (A) lymphocytic infiltrate with germinal center (A & E, ×150), (B) aggregate of mature plasma cells admixed with acute inflammatory cells (H & E, ×600), (C) fibrosis and vascular spaces resembling sclerosing hemangioma (H & E, ×150), (D) epitheloid cells (H & E, ×300), (E) spindle-shaped histiocytes with collagen fibers arranged in storiform pattern (H & E, ×150), and (F) xanthomatous area with large foam cells (H & E, ×300)

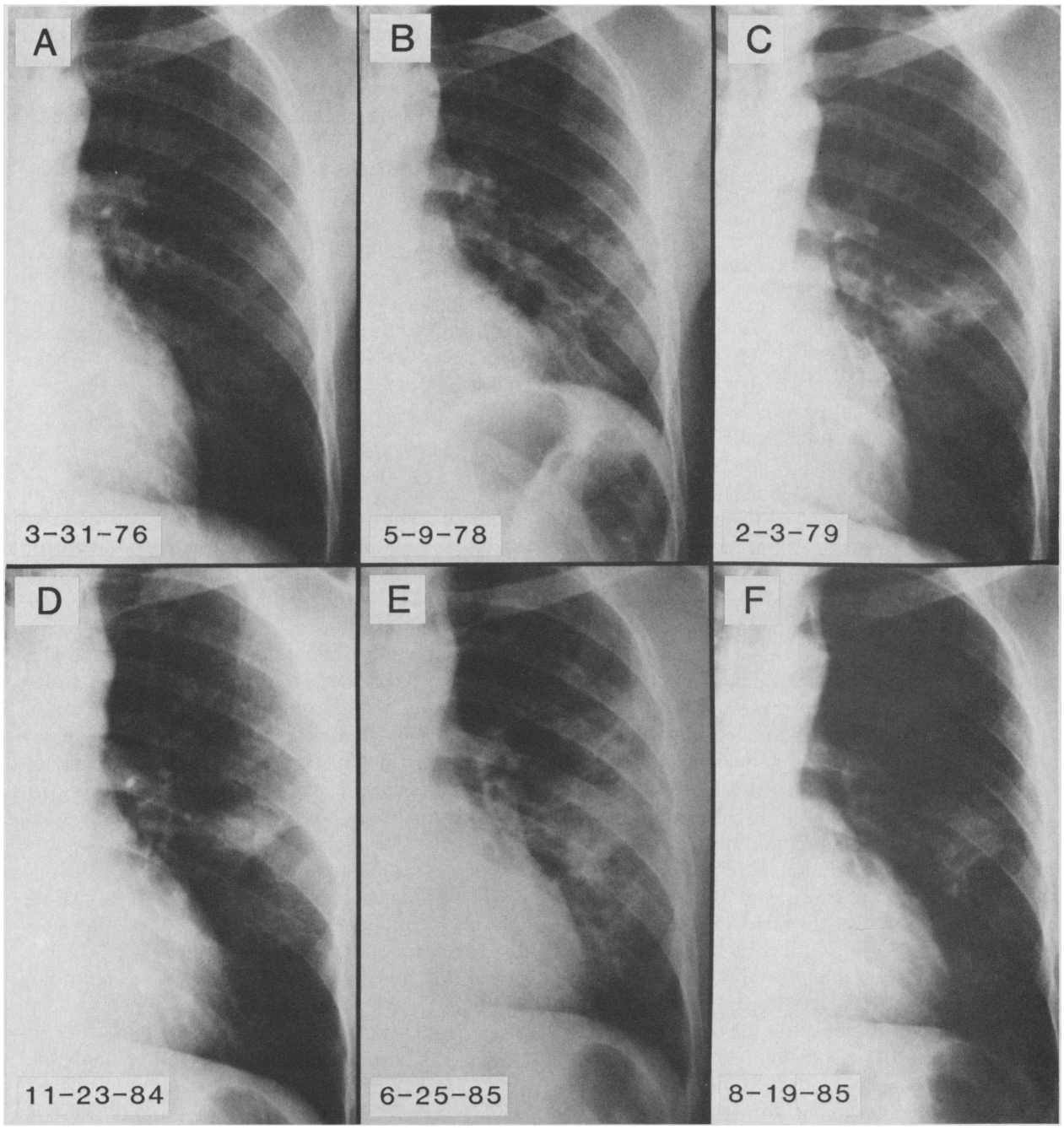

Figure 3. A series of chest x-ray films of case 2 taken at different intervals. The evolution of the lung lesion and complication of pneumonia (B and E) are revealed

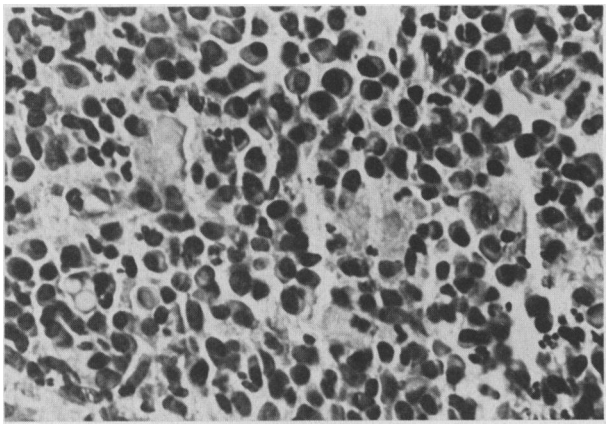

Figure 4. The lung lesion in case 2 composed primarily of mature plasma cells with easily identifiable Russell bodies

1976, was entirely normal (Figure 3A). He was treated with antibiotics and his symptoms much improved. However, in February 1979, the patient came back with sore throat, cough, chest pain, and subjective fever. A poorly defined elliptical opacity in the superior segment of lingula division of the left upper lobe was seen on chest radiograph (Figure 3C). He was again treated with antibiotics, and his symptoms subsided and the lesion shrunk.

In November 1984, the patient returned with a cough productive of blood-streaked sputum. The recurrence of the elliptical opacity in the left upper lobe was seen on chest radiograph (Figure 3D). The opacity was inhomogenous and the outline somewhat irregular. He was again placed on antibiotics. No change in the lesion was seen on a repeat chest radiograph in December 1984. The patient was doing quite well until June 1985, when he again developed cough productive of yellow-green sputum. Flaring of the opacity in the left upper lobe was revealed on chest radiograph (Figure 3E). The enlarged lesion became ill-defined and seemed to involve both anterior and lingula segments of the left upper lobe. He was then readmitted to the hospital for further evaluation and treatment.

The patient was a well-developed and well-nourished, young, black man with no positive physical signs and laboratory findings on the latest admission. Even the lungs were clear to percussion and auscultation. A skin test for tuberculosis and sputum cultures for bacteria and fungi were all negative; the same results had been obtained several times before. Bronchoscopy showed inflammation at the orifice of the lingua segment with partial obstruction. A biopsy of the lingula segment was obtained.

The biopsy specimen was composed primarily of sheets of mature plasma cells admixed with a few eosinophils and neutrophils (Figure 4). Russell bodies could be identified with no difficulty. The plasma cells were stained positive for both κ and λ light chains of immunoglobulin by the peroxidase-antiperoxidase method, indicating their polyclonal nature.

The acute process subsided after antibiotic therapy. A follow-up chest radiograph was taken in August 1985; the persistence of the opacity in the superior segment of the lingula (Figure 3F) was seen on the chest film. The patient has been free of symptoms since the last discharge, and has been followed closely by the clinic.

DISCUSSION

No etiologic agent has been identified in the inflammatory pseudotumor of the lung. Special stains and cultures for microorganisms have been negative in all reported cases, including the present two patients.[1-13] As the disease process is usually chronic and localized, the causative agent might initiate the inflammatory responses and then disappear from the lesion while the inflammation persists. On the other hand, the agent might not be detectable by the present techniques. The highly variable histologic features suggest that the lesion could be elicited by more than one kind of agent, but this might not be true because the whole spectrum of histologic features could be found in a single case as in case 1.

The principal cells involved in the response are plasma cells and histiocytes. When plasma cells are the predominant cells in the lesion as in case 2, the term "plasma cell granuloma" is commonly applied.[1,2,6,11-13] When histiocytes become predominant, "benign fibrous histiocytoma," "xanthoma," "fibroxanthoma" or "xanthogranuloma" are adopted.[7-10] The entity of "pulmonary sclerosing hemangioma" described in the literature is most likely a variant of the inflammatory pseudotumors.[8,14-17] Some lesions may contain a large number of mast cells, and thus the entity is designated as "mast cell granuloma."[18] As all the above histologic variants can be found in a single

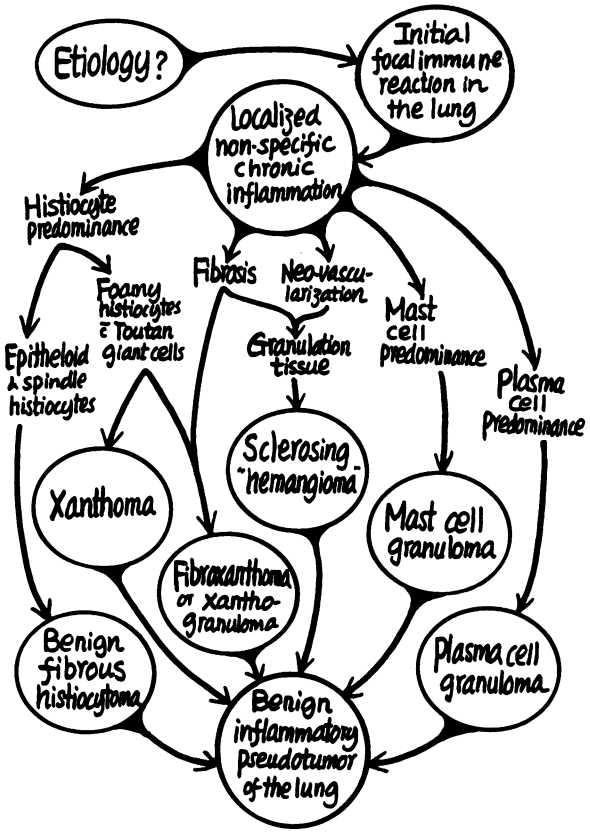

Figure 5. Diagram of a unifying hypothesis of benign inflammatory pseudotumors of the lung: various terminology reflects only the emphasis of the predominant elements in a localized, nonspecific, chronic inflammatory process

lesion as demonstrated in case 1 (Figure 2), they should be grouped together as a single entity (Figure 5).

Inflammatory pseudotumors of the lung occur more commonly in young persons: two thirds under the age of 30 years and one third under the age of 18 years. This entity is twice as common in women as in men.[1-13] Most cases are asymptomatic and are discovered incidentally as in case 1. The most common symptoms are cough, chest pain, fever, and dyspnea, all well demonstrated in case 2. The periodic flare-up of the lesion in case 2, accompanied by respiratory and constitutional symptoms, was apparently related to the pneumonia that developed as a consequence of bronchial obstruction secondary to the compression by the inflammatory pseudotumor. As soon as the pneumonia was resolved after antiobiotic treatment, the original mass lesion reappeared.

The most common radiographic finding observed in over two thirds of cases is a solitary, homogeneous, well-circumscribed, spherical or oval mass of 2 to 3 cm in diameter.[1-13] Rarely does the mass reach a size as large as 13 cm.[11] Multiple or lobulated nodules are noted only occasionally. Cavitation and endobronchial involvement are uncommon but were present in case 2. Obvious calcification of the untreated lesion is extremely rare. Nonetheless, a recent report revealed that the lesion became calcified in three patients after radiation therapy.[13] The mass is usually soft and yellow-white with occasional small brown spots of old punctate hemorrhages. The mass is discrete but not truly encapsulated.

Most inflammatory pseudotumors become stationary after the initial acute phase is over, which is usually mild and overlooked. Their differentiation from the true neoplasms and granulomatous inflammation of known etiology is important but difficult to determine, and can be certain only after biopsy and cultures. Every effort should be made to rule out the possibility of tuberculous and fungal infections. The polyclonal nature of the plasma cells should be confirmed by immunohistochemical or immunocytochemical means to rule out extraosseous plasmacytoma.

The natural history of inflammatory pseudotumors of the lung remains uncertain. Although no death has been attributed directly to the disease, and resection of the lesion results in permanent cure (case 1) the fate of the mass lesion remains unknown when left untouched. It might persist for a long time (case 2), or might heal spontaneously by fibrosis. The longer the lesion persists, the greater the chance for the following two possible complications: (1) partial or complete obstruction of bronchus because of endobronchial involvement or extrinsic compression by the mass, predisposing to either pneumonia or atelectasis,[19-21] or (2) the development of true neoplasm, particularly malignant lymphoma, because long-term stimulation of lymphocytes in chronic inflammation might lead to emergence of autonomous clone of neoplastic lymphocytes as is often observed in lymphomatoid granulomatosis and Sjögren's syndrome.[22] Therefore, if pneumonia recurs, or the lesion suddenly grows rapidly as in case 2, surgical resection or radiation therapy should be indicated.

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